

IN THE UNITED STATES PATENT OFFICE

Inventor : W. Roy KNOWLES, M.D.
Filing Date: 19 July 2000
Ser. No.: 09/619,142
Art Unit: 1614
Examiner: Vickie KIM



#8
5/9/98
2-2101

RULE 1.131 DECLARATION

- 1) I am the inventor of record for the captioned patent application. I make this declaration under 37 Code of Federal Regulations Rule 1.131.
- 2) Not later than April 14, 1996, I conceived of an invention having each of the elements of my pending patent claims.
- 3) The art, however, intimated that my combination would have adverse side effects, and possibly be ineffective. I thus needed to test it to assure that it was safe and effective for the claimed use.
- 4) I thus began testing on human volunteers, or "test subjects," various claimed combinations. I maintained a record of observations and results for each test subject. I enclose several records as exhibits. Note that on these records, I have redacted material private or not germane. The term "special minoxidil" is shorthand for a formulation described by my patent claims including minoxidil. I include case studies here encompassing a variety of formulations and concentrations within the

scope of the pending claims. To assure fullness of disclosure, I include case studies both successful and unsuccessful.

- 5) Testing Protocol. The test protocol followed was generally as follows: Informed consent of the test subject was obtained. The test subject was then given a visual demonstration of where and how much compound was to be applied. The test subject would observe the demonstration on the test subject's scalp, the test subject using a hand-held mirror to observe it. The amount of compound and locations of administration were specified until the test subject acknowledged understanding. Test subjects were instructed to telephone if they did not fully understand the instructions, or if any questions subsequently arose.
- 6) Evaluation. Test subjects were instructed to return at four-month intervals during the first year. The first visit was to determine if there might be scalp irritation. At that time, the test subject was asked to review exactly how he or she applied the test compound. Then, the entire scalp was examined using a 15-power magnifying lens, to observe if any new hairs were beginning to push through the scalp.

- 7) Usually, one could not see actual hair at four months, but could often see little black dots, which were the follicular openings beginning to enlarge prior to the hair actually beginning to show. This is analogous to seeing the ground break before a tulip pushes through the soil.
- 8) The second visit was scheduled approximately at the eight month after testing began. Compound application continued on a twice-daily basis until as much hair as could be stimulated to grow had been accomplished. This often took months, or even years, depending on factors such as the compound concentration.
- 9) Test subjects were investigated for any side effects, such as sudden weakness, feeling faint, fatigue, rapid heart beat, and sexual function or dysfunction. Any side effects were to be noted in the test record.
- 10) Results. Using this protocol, and a variety of formulation strengths, I have found several surprising things. First, testosterone blockers are not actually necessary for my invention to work; minoxidil alone is effective on 8% of patients, while the same amount of minoxidil administered with the proper amount of a penetration enhancer is effective on 35% of patients. Second, testosterone blockers added to such a mix are

synergistically beneficial, increasing the efficacy from 35% to 85% of patients. As examples, I include records from several individual test subjects.

- 11) Test Subject M.D. Not later than April 14, 1996, I began testing compounds within the pending claims on test subject "M.D." M.D. is a male, and was 42 years old at the time testing began. The redacted test record for M.D. is included as Exhibit M.D.
- 12) The test record for the initial examination says, "Mult. SK's face, scalp frozen with LN. Male pattern baldness, start special minoxidil."
- 13) I examined M.D. again, approximately four months later. The test record says that at that time, there was "Excellent response to minoxidil, has new hair all over top of scalp."
- 14) The test record reports that at the subsequent examination, M.D. "Is growing good lanago hair."
- 15) The record shows that at the subsequent examination, M.D. "Is getting good growth exp. in oce." (The term "oce" is shorthand for occipital, an area of the scalp.)
- 16) The record shows that at the subsequent examination, M.D. "Is using minoxidil twice daily. Is growing good hair in occiput."

- 17) Test Subject E.K. Not later than April 14, 1996, I began testing a compound within the scope of the claims on test subject "E.K." E.K., a male test subject, was 45 years old at the time we began testing. The redacted test record for E.K. is included as Exhibit E.K.
- 18) The test record for the initial examination says, "Male pattern baldness, has used Rogaine for approx. 5 years with fair control of hair loss. Most loss is in the occiput. The baldness comes from both sides, perhaps a little more from the father. He is very willing to use special minoxidil. ... Very minimal loss in the M Peaks to use one or two drops twice daily there." Testing began using a composition including 1% minoxidil.
- 19) The record shows that at the subsequent examination, "Minoxidil [1.0%] is producing good results at this stage. I see good black dotting across the occiput and along the existing hair on top on the parietal sides. Some early growth in front." As I mentioned earlier in this Declaration, the "black dotting" the record refers to indicates new hair growth.
- 20) The record shows that at the subsequent examination, "Hair is growing very nicely. He looks as though he has not lost any. A lot of it is minoxidil hair. I could

not point out to him with a mirror which was minoxidil vs. normal terminal hair."

21) The record shows that at the subsequent examination, the test subject "thought the minoxidil solution irritated his scalp however he is using Dial soap and perhaps was using Dial shampoo. He's not sure. The area in the occiput looks more sun induced redness than a chemical from the vehicle N."

22) Test Subject G.P. Not later than April 14, 1996, I examined test subject "G.P." G.P. is a male, 44 years old at the time we began testing. The redacted test record for G.P. is included as Exhibit G.P.

23) The test record for that initial examination says, "Male pattern baldness, would be happy to keep what hair is currently present. Given book to read on [hair] transplants, not interested at this time. To use special minoxidil." Thus, the record shows that as an alternative to hair transplant surgery, G.P. was willing to test the claimed compounds.

24) The record shows that at the subsequent examination, "Patient has had a marvelous response to Minoxidil. Original area somewhere between five and one half and six inches in diameter on vertex is now practically covered. Widest area measures two and one half inches with good

lanugo hair growing. Frontal loss has stopped. Patient and wife are extremely happy. Was in to see [] again today who pulled the pictures from five years ago where a six inch bald spot was present. [] took pictures again today; I will attempt to get copies for our records."

25) The record shows that at the subsequent examination, "Good response to Minoxidil, has grown hair in all but 1½ inch diameter area in vertex, he has good lanugo hair here."

26) The record shows that at the subsequent examination, "Excellent response with minoxidil, has a small 2" area in vertex which is not fully grown over, but has much lanugo hair."

27) The record shows that at the subsequent examination, "Has good laguno hair in the occiput. All other hair has grown out."

28) The record shows that at the subsequent examination, "Spec. minox. is holding hair well. Front looks good. Thinning spot in occ."

29) Test Subject O.D. Not later than April 14, 1996, I began testing a claimed compound on test subject "O.D." O.D., a male, was 34 years old at the time testing began. The redacted test record for O.D. is included as Exhibit O.D.

- 30) The test record for the initial examination says, "MPB [male pattern baldness], early class VI, start special minoxidil."
- 31) The record shows that at the subsequent examination, "Good growth in all areas, frontal, occipital, etc."
- 32) The record shows that at the subsequent examination, "Good growth in occiput, beginning to get good growth in frontal areas."
- 33) The record shows that at the subsequent examination, "hair in occiput is grown completely and is beginning to get good growth in frontal areas."
- 34) The record shows that at the subsequent examination, "Good hair growth from minoxidil."
- 35) The record shows that at the subsequent examination, "Is still growing good hair very well in occiput, some across top of front. Is not using Minoxidil on the very front and there is some loss about the width of an index finger. He is using it only at night, advised to continue and try to use it twice daily."
- 36) Test Subject S.J. Not later than April 14, 1996, I began testing a claimed compound on test subject "S.J." S.J., a male, was 49 years old at the time testing began. The redacted test record for S.J. is included as Exhibit S.J.

- 37) In contrast to the other test subjects discussed herein, S.J. wanted to pursue surgical hair grafting contemporaneously with compound testing. The results in this test record could thus be due to interference by the surgical hair grafts with test compound.
- 38) The test record for the initial examination says, "Male pattern baldness, to start special minoxidil, recheck in four months. [Hair] Graft not discussed, will discuss at next visit."
- 39) S.J. was examined five months later. The test record says that at that time, S.J. was "Getting good hair growth in occiput. Pore openings in frontal scalp seem to be larger, indicating to me that hair should be growing there soon. Recheck in three months. Patient desirous of discussing transplants for frontal area, no discuss[ion] today."
- 40) The record shows that at the subsequent examination, "Getting good growth in occipital area."
- 41) The test record for the visit 5 months later says, "Patient is getting thinner in frontal area."
- 42) The record shows that at the subsequent examination, "Good hair growth from minoxidil, continue."
- 43) The record shows that at the subsequent examination, "Hair has continued to fall slowly; he is still using the

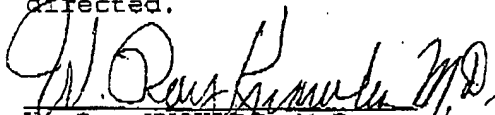
clear 1% minoxidil but only most of the time one time [daily] only. Is not overly unhappy with hair but unhappy that the balding has continued. Grafts in the frontal and top of scalp look great; do not show as grafts and are the only hair which he has, would be bald otherwise."

44) Adverse Drug Reactions. In all of the clinical testing I have done, I have had to stop administering test compound only on two occasions.

45) On one occasion, the test subject thought his heart

46) The other occasion was scalp irritation that occurred because of overuse.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United State Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon or any patent to which this verified statement is directed.


W. Roy KNOWLES, M.D.
February 5, 2001

Rule 1.131 Declaration
Inventor: KNOWLES, W.R.
Filing Date: 19 July 2000
Ser. No.: 09/619,142

EXHIBIT M.D.

NAME [REDACTED] AGE [REDACTED] DATE 11-6-[REDACTED] DR. [REDACTED]
END BILL TO [REDACTED] ADDRESS Houston, Texas 77063 PHONE [REDACTED]
EMPLOYED BY [REDACTED] REFERRED [REDACTED]
INSURANCE [REDACTED] DRIVER'S LICENSE # [REDACTED]

1-6- [REDACTED] Mult. SK's face, scalp frozen with LN. Male pattern baldness, start special minoxidil. [REDACTED]

-16- [REDACTED] Excellent response to minoxidil, has new hair all over top of scalp, cont. [REDACTED]

10-09- [REDACTED] Is growing good lanugo hair, continue Minoxidil, [REDACTED]

[REDACTED] Is getting good growth exp. in occ. [REDACTED]

8/20/ [REDACTED] Is using minoxidil twice daily. Is growing good hair in occiput. [REDACTED]

SEND BILL TO

ADDRESS HOUSTON, TEXAS 770

PHONE

EMPLOYED BY

REFERRED

INSURANCE

DRIVER'S LICENSE #

03/29/ [REDACTED] Male pattern baldness, has used Rogaine for approx. 5 years with fair control of the loss. Most loss is in the occiput. The baldness comes from both sides, perhaps a little more from the father. He is very willing to use special Minoxidil 1% filter was called into Briargrove. He will check with us in 6 months. I expect and told him so that he will get an excellent response. Very minimal loss in the M Peaks to use one or two drops twice daily there.

[REDACTED]

[REDACTED]

10/24/ [REDACTED] Minoxidil is producing good results at this stage. I see good black dotting across the occiput and along the existing hair on top on the parietal sides. Some early growth in front. Continue minoxidil, 1% filtered. Recheck in 6 months.

[REDACTED]

12/17/ [REDACTED] Hair is growing very nicely. He looks as though he has not lost any. A lot of it is minoxidil hair. I could not point out to him with a mirror which was minoxidil vs. normal terminal hair. Continue special minoxidil.

[REDACTED]

[REDACTED]

04/14/ [REDACTED] Thought the minoxidil solution irritated his scalp however he is using Dial soap and perhaps was using Dial shampoo. He's not sure. The area in the occiput looks more sun induced redness than a chemical from the

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EXHIBIT G.P.

NAME [REDACTED] AGE [REDACTED] DATE [REDACTED] OF [REDACTED]
SEND BILL TO [REDACTED] ADDRESS Houston, Texas 77062 PHONE [REDACTED]
EMPLOYED BY [REDACTED] REFERRED [REDACTED]
INSURANCE [REDACTED] DRIVER'S LICENSE # [REDACTED]

- 9-10- [REDACTED] Male pattern baldness, would be happy to keep what hair is currently present. Given book to read on transplants, not interested at this time. To use special minoxidil.
- 10-17- [REDACTED] No refill - needs X he seen. JH
- 10-28- [REDACTED] Patient has had marvelous response to Minoxidil. Original area somewhere between five and one half and six inches in diameter on vertex is now practically covered. Widest area measures two and a half inches with good lanugo hair growing. Frontal loss has stopped. Patient and wife extremely happy. Was in to see [REDACTED] again today who pulled the pictures from five years ago where a six inch bald spot was present. Barrett took pictures again today; I will attempt to get copies for our records.
- 1-25- [REDACTED] Needs X he seen. JH
- 11-28- [REDACTED] Good response to Minoxidil, has grown hair in all but 1 1/2 inch diameter area in vertex, he has good lanugo hair here, continue special Minoxidil.
- 5-26- [REDACTED] Needs to be seen. JH
- 6-1- [REDACTED] M. Thawles Oled refill for minoxidil X JH
- 06-06- [REDACTED] Excellent result with minoxidil, has a small 2" area in vertex which is not fully grown over, but has much lanugo hair. Continue. Recheck in one year or so.
- 4-6- [REDACTED] Refill of min. 12 filtered Oled to pharm. JH
- 3-8- [REDACTED] Refill of min. 12 filtered Oled to pharm. JH
- 10-07- [REDACTED] Has been out of Minoxidil for approximately one week. Has good lanugo hair in the occiput. All other hair has grown out. Refill prn for 1 1/2% filtered. Advised that this would be stronger than what he has been using.
- 7-29- [REDACTED] Pt. had been unhappy @ pharm when he gets minox. Would like to start back on it. Pres. faxed to Lifecheck. JH
- 3-01- [REDACTED] Spec. minox. is holding hair well. Front looks good. Thinning spot in occ. Cont. spl. minox. Given 1 btl.
- 2-24- [REDACTED] Faxed script to pharmacy for 5% sp Minoxidil. P.S.

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EXHIBIT O.D.

2-25-69 [REDACTED] MPB, early class VI, start special minoxidil.

6-19-69 [REDACTED] Getting good growth in all areas, frontal, occipital, etc. cont.

11-21-69 [REDACTED] Good response to Minoxidil. Growing excellent hair in occiput and good lanugo hair in frontal areas; continue.

03-18-70 [REDACTED] Good growth in occiput, beginning to get good growth in frontal areas, continue.

09-29-70 [REDACTED] [REDACTED] hair in occiput is grown completely and is beginning to get good growth in frontal areas, continue special Minoxidil BID.

10-20-70 [REDACTED] Good hair growth from minoxidil. Has run out, renew, come in when necessary or wants to.

11-16-70 [REDACTED] Is still growing good hair, very well in occiput, some across top of front. Is not using Minoxidil on the very front and there is some loss about the width of an index finger. He is using it only at night, advised to continue and try to use it twice daily.

9-11-71 [REDACTED] Minox. refused. *OK*

09/13/71 [REDACTED] Is out of minoxidil. Is using it just once daily because his formula was still the chalky type. Has good regrowth in occiput but needs b.i.d. application. Told the solution is now clear. Refilled for 1% filtered. [REDACTED]

11/24/71 [REDACTED] Hair is growing good in occiput. Continue. Will refill. [REDACTED]

5-15-72 [REDACTED] Special minox script faxed to Jan. *OK*

9-9-72 [REDACTED] Script for special minox. faxed to Jan. *OK*

12-22-72 [REDACTED] Special minox. mailed to *OK*

05/24/73 [REDACTED] Is growing good hair in occiput. Needs more. Is using it only once daily. Good frontal hair which needs b.i.d. application at least 3 times weekly. Picked up a bottle of medication today.

10-5-73 [REDACTED] Pt. called and needs more Sp. Minoxidil. [REDACTED] 5% available. Wants to try. Script for Sp. Minoxidil 5% faxed to pharmacy. *A-5*

1-31-74 [REDACTED] Script for 1 bottle of 5% Sp. Minoxidil faxed to pharmacy. *P-5*

5-2-74 [REDACTED] Script for 1 bottle of 5% Sp. Minoxidil faxed to pharmacy. *P-5*

8-15-74 [REDACTED] Script for 1 bottle of 5% Sp. Minoxidil faxed to pharmacy. *P-5*

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EXHIBIT S.J.

REFEERED

DRIVER'S LICENSE •

12-07- [REDACTED] Hair is doing fine. Will probably need additional grafts in and on top near the frontal area but not too close to the hair line, just to give more volume. [REDACTED]

SEND BILL TO

ADDRESS

PHONE

EMPLOYED BY

REFERRED

INSURANCE

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10-13- Good hair growth in occiput from minoxidil, continue.

12-20- Refill oked for refill of Minoxidil to Pharm. P.M. III

3-12- Refill oked to Pharm. 1x only for minoxidil

09-17- Hair has continued to fall slowly; he is still using the clear 1% minoxidil but only most of the time one time only. Is not overly unhappy with hair but unhappy that the balding has continued. Grafts in the frontal and top of scalp look great; do not show as grafts and are the only hair which he has, would be bald otherwise. Refill on Minoxidil prn for one year.

01/20/ Has not been using minoxidil but would like to continue. Wife to visit in 10 days.

strength to 5% and concentrate in the occipital area. To call us back in 6 weeks.

4-6- Faxed script to pharmacy for 5% Sp. Minoxidil,

6-26- Faxed script to pharmacy for 5% Sp. Minoxidil p.s.

4-12- Faxed script to pharmacy for 5% Sp. Minoxidil p.s.